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Olgu Sunumu / Case Report

Hemangiosarcoma with brain metastasis in a cocker spaniel in Türkiye

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ABSTRACT:

A 2.5 years old male English Cocker Spaniel dog was admitted to our clinic with symptoms of left axis circling, increased vocalization and vestibular ataxia. The patient's medical history revealed that the left hind limb was amputated due to a malignant tumor and the tumor type was confirmed as hemangiosarcoma by pathology report. As a result of physical, neurological and radiographic examinations, intracranial tumor metastasis of primary origin in the left hind limb was suspected. No abnormal findings were found in the cerebrospinal fluid obtained from the patient. Advanced imaging techniques (computed tomography and magnetic resonance imaging) and biopsy procedures required for treatment planning were refused by the owner and the patient died 4 days later. Macroscopic necropsy findings revealed mass foci of varying sizes in the brain, spleen, liver, diaphragm and lung. Histopathologic examination revealed hemangiosarcoma metastasis of 0.2.x0.1 cm in the brain. The post-mortem findings were consistent with the clinical findings. Brain metastasis of hemangiosarcoma in a cocker spaniel dog shows that our case is rare.

Türkiye'de cocker spaniel ırkı bir köpekte beyin metastazı ile seyreden hemanjiosarkom

ÖZET:

2.5 yaşlı erkek, English Cocker Spaniel ırkı bir köpek sol eksenli kendi etrafında dönme, vokalizasyonda artış, vestibular ataksi semptomları ile kliniğimize başvurdu. Hastanın sağlık geçmişinde sol arka ekstremitenin malign tümör kaynaklı ampute edildiği, tümör tipinin patoloji raporu ile hemanjiyosarkom olarak doğrulandığı bilgisi alındı. Yapılan fiziksel, nörolojik ve radyografik muayeneler sonucunda hastada sol arka ekstremite primer kökenli, intrakraniyal tümör metastazından şüphelenildi. Hastadan alınan beyin omurilik sıvısının yapılan incelemelerinde anormal bulguya rastlanılmadı. Tedavinin planlanması için gereken ileri görüntüleme teknikleri (bilgisayarlı tomografi ve manyetik rezonans görüntüleme) ve biyopsi işlemleri hasta sahibi tarafından reddedildi ve 4 gün sonra hasta ex oldu. Hastanın makroskobik nekropsi bulgularında başta beyin olmak üzere, dalak, karaciğer, diyafram ve akciğerde değişken boyutlarda kitlesel odaklar olduğu görüldü. Yapılan histopatolojik incelemede beyinde 0.2.x0.1 cm boyularında hemanjiosarkom metastazı görüldü. Elde edilen post-mortem bulgular klinik bulgular ile eşleşmektedir. Cocker spaniel ırkı bir köpekte hemanjiyosarkomun beyin metastazının görülmesi, olgumuzun ender olduğunu göstermektedir.

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1. Introduction

Hemangiosarcoma “hem/hemo- angio- sarcoma” is a malignant tumor that forms on the lining of blood vessels. Derived from an endothelial cell line, this highly malignant tumor is characterized by severe metastases in a short period of time (1). Commonly described in dogs, but less common in other species (2). Although hemangiosarcoma is usually reported to occur in older animals, it has also been reported to occur less frequently in younger animals (3). Although hemangiosarcoma in dogs is commonly reported in breeds such as Golden Retriever, Pointer, Boxer, Labrador Retreiver, Poodle, Siberian Husky, English Setter (1), all large breed dogs can be considered at risk. Limited success in prolonging life with surgical interventions and chemotherapeutic agents (4, 5). Hemangiosarcoma has the inherent risk of arising in any organ with blood vessels, but the most common sites reported to date are the spleen (50-65%), heart and right atrium (3-25%), subcutaneous tissues (cutaneous hemangiosarcoma) (13-17%) and liver (5-6%) (6). In a study of 85 dogs diagnosed with hemangiosarcoma, 14% of the patients were reported to have intracranial metastases and these patients usually had metastatic findings in other organs (7). Secondary brain metastases arising from primary hemangiosarcoma tumors and reaching the brain via hematogenous route are known to be rare in dogs. (8). Hemangiosarcoma in dogs is less common in cocker spaniels (9). It was aimed to contribute to the literature by presenting the clinical and pathomorphological findings of a rare case of hemangiosarcoma with brain metastasis in a cocker spaniel dog.

2. Case Story

A 2.5 years old (2 years and 7 months) English Cocker breed male dog with neurological symptoms such as circling around the left axis, inability to walk, tipping to one side, behavioral changes (increased aggression, increased vocalization) brought to Ondokuz Mayıs University Veterinary Teaching Hospital on September 2024. The dog's left posterior limb had previously been amputated. Physical examination revealed bilateral hyperplasic submandibular lymph nodes and dyspnea. Increased vocalization and moaning findings were associated with pain. On neurologic examination, threat response reflexes were negative and pupillary and palpebral reflex findings were normal. The patient had unilateral vestibular ataxia. Optic nerve (CN: II) and vestibulocochlear nerve (CN: VIII) findings were abnormal, while other cranial nerve findings were normal. Hematologic findings included mild neutrophilia and monocytosis. Urea (BUN), creatine (CREA) and alanine aminotransferase (ALT) were decreased. Mild hyperglycemia was associated with stress. Electrolyte panel (Na, K, Cl) was normal. The patient was sedated with propofol for cerebrospinal fluid (CSF) analysis (Propofol 200 mg/20 mL, Fresenius Kabi Pharmaceuticals, Istanbul, Türkiye) and intubated. CSF sample was collected with a 22-gauge black syringe tip (Tıbset®, Istanbul, Türkiye). Microscopic examination of the CSF sample revealed no pathology. Radiographic imaging revealed severe metastatic masses in the lung (Figure 1.B).

He was previously admitted on March 2024 with the complaint of limping, physical examination revealed swelling around the left femur that felt hard with palpation, and radiological examination revealed a periosteal reaction and increased surrounding soft tissue opacity in the distal left femur (Figure 1, C). A fine-needle biopsy (22-gauge black syringe tip (Tıbset®, Istanbul, Türkiye) was taken from the lesion site with suspicion of osteosarcoma. The examination showed that round or oval nucleated, shuttle-shaped neoplastic cells with limited eosinophilic cytoplasm formed irregular structures and the tumor was determined to be a sarcoma with malignant character; the origin and exact diagnosis of the tumor could not be made in the biopsy sample. For definitive diagnosis, the leg was amputated and evaluated as an excisional biopsy sample.

Shuttle-shaped neoplastic endothelial cells with oval or round nuclei, prominent multinuclei and eosinophilic cytoplasm were observed to form irregular large and small vascular structures. However, some newly formed vessels

were filled with erythrocytes and some of them were empty. After this examination, it was determined that the tumor was a hemangiosarcoma.

Figure 1: (A) Thoracic radiograph taken on the day the patient presented with limping. Images A and C are from the same time **(B)** Radiograph of the thorax at the last examination shows metastatic neoplastic nodules spreading to all lobes **(C)** radiograph of the left femur, before amputation **(D)** Radiography of the bulla tympanica for the differential diagnosis of vestibular syndrome caused by otitis media

Şekil 1: (A) *Hastanın topallama şikayetiyle başvurduğu gün çekilen toraks radyografisi. A ve C görüntüleri aynı zamana aittir* ***(B)*** *Hastanın son muayenedeki toraks radyografisi, tüm loblara yayılan metastatik neoplastik nodüller görülmektedir* ***(C)*** *Amputasyon öncesi sol femur radyografisi* ***(D)*** *Otitis media kaynaklı vestibüler sendromun ayırıcı tanısı için bulla timpanika radyografisi*

At our examination in September, we suspected that the main source of the patient's clinical symptoms was the primary leg-focused (Figure 1.C) intracranial metastasis diagnosed in March. The findings indicated that computed tomography (CT) and cranial-focused magnetic resonance imaging (MRI) were necessary to understand the spread and severity of the metastasis to other organs. The imaging and biopsy procedures required to determine whether the newly formed mass foci were hemangiosarcoma metastases or a different mass formation were refused by the owner and the patient died 4 days after admission to our hospital.

Post-mortem findings

The abdominal cavity was opened and nodular, dark red masses of varying sizes and diameters were observed on the spleen (Figure 2.A) and liver (Figure 2.B). Adhesions between the liver and diaphragm were noted. When the thoracal cavity was opened, a large, white and firm masses of varying sizes were seen in the lung (Figure 2.D). There was also a dark structure on the apex of the heart. Skull was opened and 2 bilateral masses were detected dorsally in the hemispheres (Figure 2.C). Other brain regions appeared normal.

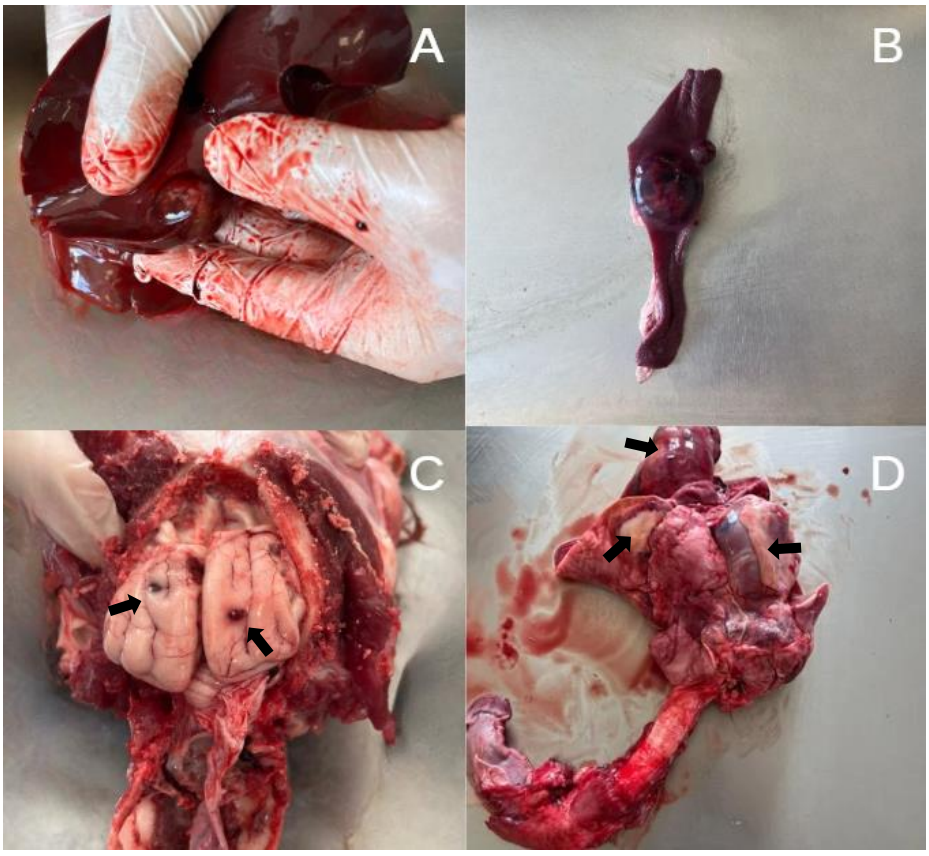

Figure 2: (A) Approximately 1x1 cm massive node localized in the right anterior lobe of the liver **(B)** Two masses on the parietal surface of the spleen, approximately 2x1.5 and 0.5x0.5 cm in the mid-anterior region **(C)** Superficial, approximately 0.2x0.1cm masses in the dorsal part of the brain, on both hemispheres, superficial to the sulcus marginalis (arrows) **(D)** Variable size of masses in the lung (arrows)

***Şekil 2**: **(A)** Karaciğerin sağ ön lobunda lokalize yaklaşık 1x1 cm'lik kitlesel nodül **(B)** Dalağın parietal yüzeyinde, orta-ön bölgede yaklaşık 2x1,5 ve 0,5x0,5 cm'lik iki kitle **(C)** Beynin dorsal kısmında yüzeysel, yaklaşık 0,2x01. Beynin dorsal kısmında, her iki hemisferde, sulkus marginalis yüzeyinde 1 cm'lik kitleler (oklar) **(D)** Akciğerde değişken büyüklükte kitleler (oklar)*

After necropsy, tissue samples were fixed in 10% formaldehyde, implanted in paraffin, sectioned at 5 µm thickness and stained with Hematoxylin-Eosin (HxE). The histopathologic appearance of the masses seen microscopically in the liver (Figure 3.A), lung (Figure 3.B), diaphragm (Figure 3.C) and brain (Figure 3.D) was determined as hemangiosarcoma as in the previous biopsy sample. Accordingly, the tumor in the leg region was the primary focus and the structures in the organs examined were determined to be metastatic foci of this tumor.

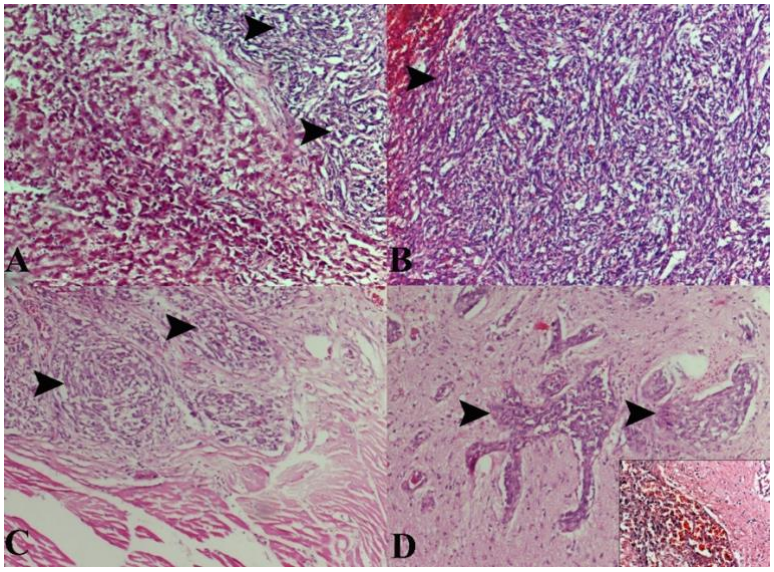

Figure 3: (A) Focus of metastatic tumor cells in the liver (arrowheads). Intact hepatocytes are seen in the right border, HxE **(B)** Tumor cells diffusely infiltrated into lung tissue (arrowhead), HxE **(C)** Tumor cell focus (arrowheads) located in the periphery of the diaphragm muscles, HxE. **(D)** Focal focuses of metastases in the brain (arrowheads) HxE. X10 objective magnification. Inset: Neoplastic vascular structures filled with erythrocytes. Brain, HxE. X20 objective magnification.

Şekil 3: (A)*Karaciğerde bulunan metastatik tümör hücresi odağı (okbaşları). Hemen komşu sınırında bulunan sağlam kalmış hepatositler görülmektedir, HxE* ***(B)*** *Akciğer dokusuna diffuz şekilde infiltre olmuş tümör hücreleri (okbaşı), HxE* ***(C)*** *Diyafram kaslarının periferinde bulunan tümör hücresi odağı (okbaşları), HxE* ***(D)*** *Beyinde fokal metastaz odakları (okbaşları) HxE. X10 objektif büyütme. İnset: İçleri eritrositle dolu neoplastik damar yapıları. Beyin, HxE. X20 objektif büyütme*

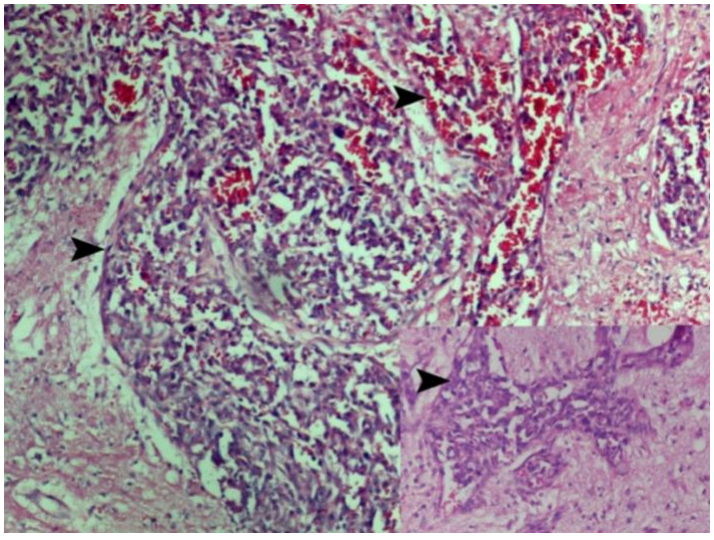

Figure 4: Brain metastasis of haemangiosarcoma. Neoplastic vessels filled with erythrocytes or empty in the lumen (arrows). x10 magnification. Inset: Neoplastic cells form capillary-like vessels (arrow). x20 magnification.

Şekil 4: *Hemanjiosarkomun beyin metastazı. Eritrositlerle dolu veya lümeni boş neoplastik damarlar (oklar). x10 büyütme. İnset: Neoplastik hücreler kapiller benzeri damarlar oluşturur (ok). x20 büyütme.*

3. Discussion and Conclusion

Hemangiosarcoma has an aggressive metastatic character. Survival is not long and prognosis is poor despite medical and operative treatments. Although hemangiosarcoma is reported to be more common in German Shepherd dogs, Boxers and Golden Retrievers and less common in English Cocker Spaniels (9), our case was reported in a Cocker Spaniel. In a study published in 1985, the mean age of 104 dogs diagnosed with hemangiosarcoma was 10 years (1). In the study published in 2013, the mean age of 51 dogs diagnosed with hemangiosarcoma was 10.7 years, the youngest patient was 5 years old (10). In the most recent report, it was stated that although the cases are mostly seen in the age range of 7-15 years, it can also be seen less frequently in young animals 2 years and older (11). In fact, a case of primary cerebrum-focused hemangiosarcoma in a 6-week-old dog has been reported and it is clear that the tumor can be seen at any age (12). In the studies conducted since 1985, the median age of patients diagnosed with hemangiosarcoma has not changed. In addition, the fact that our patient was a 2.5-year-old is rare case according to the current literature. In hemangiosarcoma in the leg, which was the primary tumor focus, metastasized to other abdominal organs, lung and the brain within 6 months, confirming the severe metastatic character of the tumor and the poor prognosis. It can be considered as stage- III in the clinical classification of hemangiosarcoma, especially because the mass foci in the lung are 5 cm in diameter, have long distance metastasis from the primary focus, and have a short life expectancy (13). In dogs with splenic hemangiosarcoma, the mean survival time of patients who underwent splenectomy was reported to be between 19 and 86 days. Considering that 31% of the patients had a survival time of 2 months and 7% had a survival time of 1 year in the postoperative period, it is clear that the current treatment options are inadequate (2).

The fact that hemangiosarcoma originates from endothelial cells on the inner surface of blood vessels and lymph vessels and can easily metastasize through the circulation leads to the risk of intracranial metastasis. In 2022, 14.2% of reported hemangiosarcoma cases had intracranial metastases (14), and 14% of reported hemangiosarcoma cases had intracranial metastases in a retrospective study conducted in 1985 (1), it can be assumed that brain metastasis rates have not changed from past to present and brain metastases can be seen in 14%-14.2% of hemangiosarcoma patients. Our patient had left-axis circling movement and vestibular ataxia, absence of threat response reflex, CN: II and CN: VIII cranial nerves were abnormal. The intracranial lesion sites were located in the pars orbitalis of the procencephalon, at the level of the parietal lobes of both hemispheres, and medial to the sulcus marginalis, explaining the neurological symptoms seen. increased vocalization was associated with mental impairment and pain due to vestibular dysfunction. Similar neurological symptoms to our case were noted in a case with lesions in the left ventricle and cerebrum and cerebral hemorrhage due to hemangiosarcoma (15). The presence of neurological symptoms in 6 of 17 patients with intracranial hemangiosarcoma (7), indicates that neurological symptoms may vary according to the localization and size of metastatic lesions in the brain.

In recent years, cases of perivulvar (Rottweiler/11 years/ Female) (16), perianal (Doberman Pinscher/5 years/ Male) and mesenterial (mongrel/6 years/ Female) (17), perianal (Doberman Pinscher/5 years/ Male) and mesenterial (mongrel/6 years/ Female) (18) hemangiosarcoma have been reported in Türkiye. Our case is rare because it was observed in a cocker spaniel, a breed of dog in which hemangiosarcoma is less common, and it was accompanied by brain metastasis.

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Conflict of Interests

The authors declared that there is no conflict of interest.

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Authors' Contributions

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Analysis and/ or interpretation: Muhammed Taha KAYA, Şamil Buğra KÖSE
Literature review: Şamil Buğra KÖSE
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Critical review: Zeynep Nurselin KOT

Ethical Approval

The data, information and documents presented in this article have been obtained within the framework of academic and ethical standards. Ethical statements have been obtained from the authors, affirming that all information, documents, evaluations, and conclusions are presented in accordance with scientific ethical and moral principles.

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